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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,497	02/17/2000	DAVID J. FITZGERALD	015280-317100US	4036

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/381,497	FITZGERALD ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/02/2007 has been entered.

2. Claims 1-56 and 58-72 have been cancelled.

3. Claim 57 is under examination.

Rejections Withdrawn

4. The rejection of claims 1-4, 7-11, 13-14, 16-17 and the newly added claims 70-72 under 35 U.S.C. 103(a) as being unpatentable over Ghetie et al (Cancer Res. 51:5876-5880, 1991) and in view of Shen et al (Int. J. Cancer 42:792-797, 19882) and Reiter et al (Biochemistry 33:5451-5459, 1994) and Kuan et al (Biochemistry 35:2872-2877, 1996, Abstract published 2/1/96) and Orlandi et al (Proc. Natl. Acad. Sci. USA, 86:3833-3837, 1989), Cabilly et al (U.S Patent 4816567, issued 3/89), Boss et al (U.S Patent 4816397, issued 3/89), Robinson et al (U.S. Patent 5618920, filed 4/94), Ward et al (Nature 341:544-546, 1989), and Huston et al (U.S. Patent 5258498, issued 11/93) is withdrawn in view of the cancellation of the claims.

5. The rejection of claims 58-69 under 35 U.S.C. 103(a) as being unpatentable over Ghetie et al (Cancer Res. 51:5876-5880, 1991) and further in view of Shen et al (Int. J. Cancer 42:792-797, 1988) and Reiter et al (Biochemistry 33:5451-5459, 1994) and Kuan et al (Biochemistry 35:2872-2877, 1996, Abstract published 2/1/96) is withdrawn in view of the cancellation of the claims.

Rejections Maintained

6. Claim 57 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Ghetie et al (Cancer Res. 51:5876-5880, 1991; of record in the office action mailed 11/02/2000) and further in view of Shen et al (Int. J. Cancer 42:792-797, 1988; of record in the office action mailed 05/08/2002) and Reiter et al (Biochemistry 33:5451-5459, 1994; of record in the office action mailed 11/02/2000) and Kuan et al (Biochemistry 35:2872-2877, 1996, Abstract published 2/1/96; of record in the office action mailed 11/02/2000).

The applicants argue that surprising results were obtained using RFB4dsFv-PE38 in Phase I clinical trials for the treatment of hairy-cell leukemia (pages 3-4 of the response filed 11/02/2007).

The above arguments are carefully considered but are not found persuasive. In response, the applicant is directed to MPEP 716.01 (C) I and II wherein it states that

> Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). See also In re Lindner, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); Ex parte George, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991).
>
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP § 2145 generally for case law pertinent to the consideration of applicant's rebuttal arguments.

The argument presented by the applicant is not found persuasive to be unexpected and unobvious and hence is considered to be moot.

The statement that the inventors were surprised at how good the results were and at how quickly, for most, patients, complete remission was achieved, in addition to an article from the ACS News Center (Appendix A), are not adequate evidence to outweigh the evidence of obviousness found in the references. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of a *prima facie* case was reached, not against the conclusion itself. *In re Eli Lilly*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990). In other words, each piece of rebuttal evidence should not be evaluated for its ability to knockdown the *prima facie* case. All of the competent rebuttal evidence taken as a whole should be weighed against the evidence

supporting the *prima facie* case. *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984). . Although the record may establish evidence of secondary considerations which are indicia of nonobviousness, the record may also establish such a strong case of obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness. Newell Cos. v. Kenney Mfg. Co., 864 F.2d 757, 769, 9 USPQ2d 1417, 1427 (Fed. Cir. 1988), cert. denied, 493 U.S. 814 (1989); Richardson-Vicks, Inc., v. The Upjohn Co., 122 F.3d 1476, 1484, 44 USPQ2d 1181, 1187 (Fed. Cir. 1997).

Applicant's claimed surprising result and the expectation of the successful clinical trial of the RFB4 dsFv antibody conjugated with PE-38, in patients with hairy-cell leukemia, is *prima facie* obvious to one of ordinary skill in the art because the evidence submitted does not prove any results beyond what one of ordinary skill in the art might have expected, and since the references strongly suggest RFB4 dsFv conjugated to PE-38 would be an excellent candidate for the treatment of hairy-cell leukemia. As discussed in the previous Office Action, Ghetie et al teach the inhibition of the growth of B-cell lymphomas comprising anti-CD22 antibody, Shen et al teach the hybridoma producing RFB4 antibody and Reiter et al teach recombinant immunotoxins comprising disulfide stabilized antibody with a cysteine at position 44 in the VH and a cysteine at position 100 in the VL, conjugated to the *Pseudomonas exotoxin*, PE38, providing a clear and strong motivation that the disulfide stabilized RFB4 antibody would be an ideal candidate for treating B-cell lymphomas. Further, Shen et al clearly teach (pages 795-796 Discussion, in particular) that the unusually potent cytotoxic activity of the disulfide

stabilized RFB4 antibody would be excellent candidates for the systemic therapy of $CD22^+$ human B-cell neoplasm; for example hairy-cell leukemia in addition to making effective reagents for the in vivo therapy of $CD22^+$ B cell lymphomas and leukemia in humans. Thus, the references on their face lead to a general expectation of a clinical success in inhibiting the growth of a hairy-cell leukemia cell that express a CD22 molecule. It is noted that the Appendix A states that the drug is highly effective in hairy cell leukemia; however, a skilled artisan would have had reasonable expectation of such result by combining the teachings above. The evidence submitted does not prove any results beyond what one of ordinary skill in the art might have expected adequate to rebut the *prima facie* case of obviousness. *Ex parte The Nutrasweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991). See MPEP 716.02(a).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

7. No claims are allowed

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
Ph: (571) 272-8789

DAVID J. BLANCHARD
~~PATENT~~ EXAMINER
PRIMARY